

SA

CA

[illegible]

United States Patent [19]

Barrows et al.



[11] Patent Number: 5,583,114

[45] Date of Patent: Dec. 10, 1996

[54] ADHESIVE SEALANT COMPOSITION

[75] Inventors: Thomas H. Barrows, Cottage Grove;
Terry W. Lewis, Woodbury; Myhanh
T. Truong, Blaine, all of Minn.

[73] Assignee: Minnesota Mining and
Manufacturing Company, Saint Paul,
Minn.

[21] Appl. No.: 281,473

[22] Filed: Jul. 27, 1994

[51] Int. Cl.⁶ A61K 38/00; A61K 39/00;
C07K 1/00

[52] U.S. Cl. 514/21; 514/2; 514/4;
530/362; 530/363; 530/366; 530/830; 424/77;
424/78.02; 424/78.06; 424/179.1; 424/193.1;
424/194.1; 424/422; 424/423; 424/428;
525/54.1

[58] Field of Search 514/21, 2, 4; 530/350,
530/362, 363, 366, 830; 424/77, 78.02,
78.06, 422, 423, 428; 524/54.1

[56] References Cited

U.S. PATENT DOCUMENTS

2,688,610	9/1954	Elins et al.	260/117
4,101,380	7/1978	Rubinstein et al.	530/350
4,163,097	7/1979	Baumann et al.	525/531
4,356,819	11/1982	Potaczek	128/156
4,416,314	11/1983	Battista	260/117
4,670,417	6/1987	Iwasaki et al.	514/6
4,692,462	9/1987	Banerjee	514/449
4,839,345	6/1989	Doi et al.	514/21
4,851,513	7/1989	Devore et al.	530/356
5,162,430	11/1992	Rhee et al.	525/54.1
5,385,606	1/1995	Kowanko	106/124

FOREIGN PATENT DOCUMENTS

0194807A3	9/1988	European Pat. Off.
2551660	3/1985	France
WO90/13540	11/1990	WIPO
WO92/02238	2/1992	WIPO
WO94/03155	2/1994	WIPO

OTHER PUBLICATIONS

Abuchowshi et al., *The Journal of Biological Chemistry*, vol. 252, No. 11, pp. 3578-3581, Jun. 10, 1977.
D'Urso et al., *Biotechnology Techniques*, vol. 8, No. 2, pp. 71-76, Feb. 1994.

Two-Component Fibrin Sealant Tisseel® Kit Brochure.

Abstract, Abdella et al., "A New Cleavable Reagent Cross-linking and Reversible Immobilization of Protein", *Biochem. Methods*, 91:16228v, 1979.

Kalman et al., "Synthesis of a Gene for Human Serum Albumin and Its Expression in *Saccharomyces cerevisiae*", *Nucleic Acids Research*, vol. 18, No. 20, 1990, pp. 6075-6081.

Sleep et al., "The Secretion of Human Serum Albumin from the Yeast *Saccharomyces cerevisiae* Using Five Different Leader Sequences", *Bio/Technology*, vol. 8, Jan. 1990, pp. 42-46.

Sijmons et al., "Production of Correctly Processed Human Serum Albumin in Transgenic Plants", *Bio/Technology*, vol. 8, Mar. 1990, pp. 217-221.

Quirk et al., "Production of Recombinant Human Serum Albumin from *Saccharomyces cerevisiae*", *Biotechnology and Applied Biochemistry*, 11, 273-287 (1989).

D'Urso et al., "New Hydrogel Based on Polyethylene Glycol Cross-Linked with Bovine Serum Albumin", *Biotechnology Techniques*, vol. 8, No. 2 (Feb. 1994) pp. 71-76.

Primary Examiner—Elizabeth C. Weimar

Assistant Examiner—Abdel A. Mohamed

Attorney, Agent, or Firm—Gary L. Griswold; Walter N. Kirm; Paul W. Busse

[57] ABSTRACT

This invention is related to an adhesive composition which may be used to bond or seal tissue in vivo. The adhesive composition is readily formed from a two component mixture which includes a first part of a protein, preferably a serum albumin protein, in an aqueous buffer having a pH in the range of about 8.0-11.0 and a second part of a water-compatible or water-soluble bifunctional crosslinking agent. When the two parts of the mixture are combined, the mixture is initially a liquid which cures in vivo on the surface of tissue in less than about one minute to give a strong, flexible, pliant substantive composition which bonds to the tissue and is absorbed in about four to sixty days. The adhesive composition may be used either to bond tissue, to seal tissue or to prevent tissue adhesions caused by surgery.

17 Claims, 3 Drawing Sheets